REMARKS

Applicant recognizes with appreciation that Examiner indicates that Claim 13 would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims.

In this Amendment, Applicant has amended Claims 10, 13 – 15 and 20 to specify different embodiments of the present invention and overcome the rejection, and cancelled Claims 11, 12 and 26, without prejudice or disclaimer. It is respectfully submitted that no new matter has been introduced by the amended claims. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

CLAIM OBJECTIONS:

Claims 12 – 14 and 20 have been objected as containing certain informalities.

It is respectfully submitted that the objection has been overcome by the amendment. More specifically, Claim 12 has been cancelled without prejudice or disclaimer. Claims 13 and 14 have been amended to spell out the abbreviated terms such as EPA and DHA. Claim 20 has been amended to add "acid" after respective group members. Therefore the objection has been overcome and withdraw of the objection is requested.

REJECTIONS UNDER 35 U.S.C. § 112 FIRST PARAPGRAPH:

Claims 15 and 17 – 20 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 12 and 14 – 23 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly

failing to enable any person skilled in the art to which it pertains to practice the invention commensurate in scope with these claims.

It is respectfully submitted that in view of the presently submitted amendments, the rejection has been overcome. In particular, Claim 12 has been cancelled without prejudice or disclaimer. In addition, Claim 15 have been amended to specify "An oral pharmaceutical composition comprising 13-hydroxyoctadeca-9Z, 11E-dienoic acid (13-HODE) in its free form and at least one pharmaceutically acceptable carrier." Claims 17 and 20 also include this feature by their dependence on Claim 15. As pointed out by the Examiner, the combination as defined in the amended Claim 15 is adequately supported by the specification.

Furthermore, Claims 14 has been amended to "at least one omega-3 fatty acid selected from the group consisting of ethyl-eicosapentaenoic acid and ethyl-docosahexaenoic acid". Such feature is also adequately described in the specification to enable any person skilled in the art to which it pertains to practice the invention commensurate in scope with these claims.

Therefore, the rejection under 35 U.S.C. § 112, first paragraph has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112 SECOND PARAPGRAPH:

Claims 10 and 20 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is respectfully submitted that the amended Claim 10 clearly point out and define the embodiment of the present invention. At first, the "may occur" in Claim 10 has been amended to "occurs" to clearly point out and define the embodiments of the present invention. In addition, Claim 20 has been amended to spell out "docosahexaenoic acid".

Therefore, the rejection under 35 U.S.C. § 112, second paragraph, has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested.

REJECTIONS UNDER 35 U.S.C. §103:

Claims 14 – 23 and 26 have been rejected under 35 U.S.C. §103 as allegedly being unpatentable over by Vanderhoek et al. (US 6,077,525), hereinafter Vanderhoek, in view of Breivik et al. (US 5,502,077), hereinafter Breivik.

Applicant traverses the rejection and respectfully submits that the embodiments of present-claimed invention are not obvious over Vanderhoek in view of Breivik. At first, Claim 26 has been cancelled without prejudice or disclaimer. Thus, the rejection to Claim 26 is moot. In addition, Claims 14 has been amended to "at least one omega-3 fatty acid selected from the group consisting of ethyl-eicosapentaenoic acid and ethyl-docosahexaenoic acid". Claims 16 and 21 – 23 also include this feature due to their dependency on Claim 14. Claim 15 have been amended to specify "An oral pharmaceutical composition comprising 13-hydroxyoctadeca-9Z, 11E-dienoic acid (13-HODE) in its free form and at least one pharmaceutically acceptable carrier." Claims 17 – 20 also include this feature by their dependence on Claim 15.

It is respectfully submitted that a person of ordinary skill in the field of thrombosis, vascular disease and its treatment would recognize that the underlying etiology is multi-factorial, involving hypercoagulability, platelet activation, inflammation and vascular dysfunction. This same person would know that all of these are exacerbated by specifically known risk factors, including smoking, hyperlipidermia, hypertension, and diabetes, (Mehta *et al.*, J. Am. Coll. Cardiol. 31: 1217, 1998; Karp *et al.*, Am. J. Epid. 160: 707, 2004; Satter *et al.*, Circ., Oct. 18, 2004; Yusuf *et al.*, Lancet 364: 937, 2004). Moreover, such a person would recognize that simply lowering cholesterol, decreasing hypertension, impairing platelet function or treating diabetes alone **will not** prevent vascular disease (Ascaso *et al.*, Am. J. Cardiovasc. Drugs 4: 299, 2004; Yusuf,

Am. Heart J. 148:52, 2004; Morimoto *et al.*, Am. J. Med. 117: 459, 2004; Briel *et al.*, Am. J. Med. 117: 596, 2004). In addition, most current treatments, particularly anti-platelet agents and anti-coagulants place patients have the risk of bleeding and hemorrhagic stroke.

Therefore, (cardio)vascular disease is a multi-factorial entity that requires a combination of drug treatments to attenuate its progression. From the perspective of anti-platelet agents such as aspirin and GPIlbIIIa inhibitors, which have been shown to attenuate acute and short-term myocardial infarctions and thrombotic stroke (Aspirin Trialists Collaboration, Br. Med. J. 308: 159, 1994; The EPILOG Investigators, N Engl. J. Med. 336: 1689, 1997). These agents do not prevent vascular wall hyperplasia, (re)stenosis or alter vascular wall biocompatibility. In fact, there is no currently used antithrombotic agent that prevents vascular wall hyperplasia, (re)stenosis or alters vascular wall compatibility.

Vanderhoek provides a single example of a highly complex formulation of 9, 11 octadecadienoic in combination with many different ingredients including monoglyceride (see Example 3). However, 9, 11 octadecadienoic is a different compound from 13-HODE. Moreover, Figure 3 of Vanderhoek teaches away from the use of 13-HODE as an inhibitor of platelet aggregating TXB_2 formation compared to 13-HODE. Therefore, Vanderhoek does not disclose the combination of 13-HODE in a simple mixture with either a glyceride or an ethyl ester nor does it suggest that such formulations would be useful for treating cardiovascular and related disease. By reading EP 0 955 047, the skilled artisan would not be led to formulations containing 13-HODE with a glyceride or an ethyl ester.

The Examiner states that Vanderhoek and Breivik teach the use of conjugated fatty acids including ethyl-EPA, 13-HODE, and antioxidants for inhibiting platelet aggregation and it would be obvious to a person of ordinary skill in the relevant art to configure some combination thereof to optimize vascular wall biocompatibility. Applicant respectfully disagrees with the Examiner and submits that the current invention is not obvious over Vanderhoek in view of Breivik. More specifically, a person of

ordinary skill in the art would know that omega-3 fatty acids that prevent platelet aggregation *in vitro* or *ex vivo* provide **no clinical benefit** to patients with (cardio)vascular disease (The EMPAR Study, Cairns et al. Circ. 94: 1553, 1996). These investigators demonstrated in clinical trials that conjugated dietary fatty acids thought to attenuate platelet function have **no effect** on the reduction of coronary (re)stenosis in patients undergoing percutaneous transluminal coronary angioplasty. Other investigators have reported that increased levels of 13-HODE are associated with **increased atherogenesis** (Feinmark & Cornicelli, Biochem. Pharmacol. 54: 953, 1997; Ylä-Herttuala et al., Proc Natl Acad Sci USA 87: 6959, 1990; Ylä-Herttuala et al., J. Clin. Invest: 95: 2692, 1995). Therefore, a person of ordinary skill in the art would be faced with the conundrum that the literature indicates that anti-platelet agents *per se* have no benefit on vascular biocompatibility, and 13-HODE, in particular, appears to have detrimental effects. Thus, the prior art teaches away from the use of instantly claimed compositions as having both an "anti-platelet effect" and "a vascular effect".

Finally, a person skilled in the art would realized that all prior art antithrombotic treatments, including those taught by Vanderhoek and Breivik, impact significantly on coagulation and/or platelet function and render platelets hemostatically dysfunctional; i.e., place the patient at risk of bleeding. The present invention focuses on vascular wall biocompatibility; i.e., returning the vessel wall to hemeostatis conditions **without rendering the patient hemostatically dysfunctional.** Therefore, the embodiments of the present invention as claimed are different from the disclosures in Vanderhoek and Breivik.

Therefore, the rejection under 35 U.S.C. §103 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. §103 is respectfully requested.

Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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